forms. The transmembrane glycoprotein of Ebola viruses is unusual in that it is encoded in two open reading frames. Expression of GP occurs when the 2 reading frames are connected by transcriptional or translational editing (Sanchez et al., Proc. Natl. Acad. Sci. USA 93; 3602-3607, 1996; Volchkov et al., Virology 214, 421-430, 1995). The unedited GP mRNA produces a non-structural secreted glycoprotein (sGP) that is synthesized in large amounts early during the course of infection (Volchkov et al., 1995, supra; Sanchez et al., 1996, supra; Sanchez et al., J. Infect. Dis. 179 (suppl. 1, S164, 1999). Following editing, the virion-associated transmembrane glycoprotein is proteolytically processed into 2 disulfide-linked products (Sanchez et al., J. Virol. 72, 6442-6447, 1998). The amino-terminal product is referred to as GP1 (140 kDa) and the carboxy-terminal cleavage product is referred to as GP2 (26 kDa). GP1 and membrane-bound GP, covalently associate to form a monomer of the GP spike found on the surfaces of virions (V E. Volchkov et al., Proc. Natl. Acad. Sci. U.S.A. 95, 5762, 1998; A. Sanchez et al., J. Virol. 72, 6442,1998). GP1 is also released from infected cells in a soluble form (V E. Volchkov. et al., Virology 245, 110, 1998). sGP and GP1 are identical in their first 295 N-terminal amino acids, whereas the remaining 69 C-terminal amino acids of sGP and 206 amino acids of GP1 are encoded by different reading frames. It has been suggested that secreted GP1 or sGP may effectively bind antibodies that might otherwise be protective (Sanchez el al., 1996, supra; Volchkov el al. 1998, supra).

[0012] Ebola virus GP is a Type I transmembrane glycoprotein. Comparisons of the predicted amino acid sequences for the GPs of the different Ebola virus strains show conservation of amino acids in the amino-terminal and carboxy-terminal regions with a highly variable region in the middle of the protein (Feldmann el al., Virus Res. 24: 1-19,1992). The GP of Ebola viruses are highly glycosylaled and contain both N-linked and O-linked carbohydrates that contribute up to 50% of the molecular weight of the protein. Most of the glycosylation sites are found in the central variable region of GP.

[0013] GP is expressed as a 676 amino acid precursor that is post-translationally cleaved by furin to yield two subunits, GP1 and GP2 (11). GP1 and GP2 remain covalently linked by a disulfide bond (12), and the resulting GP1-GP2 pair trimerizes to yield a ~450 kDa envelope spike on the viral surface. GP1 is responsible for attachment to new host cells while GP2 mediates fusion with those cells. GP1 also serves as a hydrophobic clamp on GP2, holding it in its metastable, pre-fusion conformation on the viral surface. When the clamp is released during entry, GP2 is thought to undergo irreversible conformational changes that drive fusion with host endosomal membranes (13, 14). Although a definitive receptor has yet to be identified for the ebolaviruses, virions can enter cells through an endocytic pathway (15-18). A key step in this pathway appears to be cleavage of a flexible loop containing GP1 residues 190-213 (19, 20), by endosomal cathepsins (15-17). Several neutralizing mAbs have been raised against ZEBOV (5, 7-10), but it is not yet known at what stage of entry these antibodies function.

[0014] Other studies have also demonstrated limited efficacy of passively transferred polyclonal antibodies in protection against Ebola challenge (Mikhailov et al, 1994, Voprosi Virusologii, 39, 82-84; Jahrling et al., 1996, Arch Virol, US, 135-140; Jahrling et al., 1999, J Infect Dis, 179 (Suppl 1), S224-234; Kudoyarova-Zubavichene et al., 1999, J Infect Dis, 179 (Suppl 1), S218-223). However, it is difficult to determine the effective therapeutic dose of antibodies in different preparations of polyclonal antibodies. Efforts to identify the role of antibodies in protection led to the isolation of monoclonal antibodies from mice vaccinated with Ebola GP (for instance, U.S. Pat. Nos. 6,630,144; 6,875,433; 7,335,356; and Wilson et al. Science 287, 1664, 2000), and from convalescent people (Maruyama et al. J. Infect. Dis. 179 (suppl 1), S235, 1999; Maruyama et al. J. Virol. 73, 6024, 1999; Parren et al. J. Virol 76, 6408, 2002). These were tested in rodents and protected against lethal infection (Wilson et al. Science 287, 1664, 2000; Parren et al. J. Virol 76, 6408, 2002).

[0015] Therefore, there exists a need for antibodies reactant to the Sudan Boniface virus and means to produce the same so that the virus may be detected and methods of treatment and prophylaxis against the same may be developed.

SUMMARY OF THE INVENTION

[0016] Monoclonal antibodies (MAbs) against glycoproteins (GPs) of the Ebola Sudan Boniface Virus are disclosed, as are hybridoma cells which produce the same. A crystal structure of the trimeric, prefusion Sudan ebolavirus glycoprotein, in complex with a novel Sudan ebolavirus-neutralizing antibody, illustrates a shared structural epitope which could be a "sweet spot" for neutralizing the ebolaviruses. These MAbs were protective against Ebola Sudan Boniface Virus challenge when administered prophylactically or therapeutically. (By "prophylactic", it is meant administered before challenge, and by "therapeutic", it is meant administered after challenge.)

[0017] The invention of these monoclonal antibodies that recognize the glycoprotein of Sudan Boniface mark the first time to our knowledege that a reagent has been developed that will specifically identify Ebola Sudan Boniface.

[0018] The monoclonals generated in this disclosure are the only known Sudan specific monoclonal antibodies. This invention will allow a scientist to specifically recognize the Sudan Boniface species of Ebola Virus in an outbreak situation.

[0019] Cross-reactivity across all the Ebola and Marburg viruses is not present. Therefore, a diagnostic or therapeutic medical countermeasure against one Ebola strain will not cross react with another Ebola strain. It is therefore prudent to have as many monoclonal antibodies (MAbs) MAbs in the art as possible to ensure a wide variety of MAbs against Ebola virus infections.

[0020] One embodiment of this invention relates to monoclonal antibodies that protect against Ebola Sudan Boniface virus and bind to epitopes on the virus GP.

[0021] Another embodiment relates to the sequences of these monoclonal antibodies, in particular, the sequences to MAbs: 16H11, 19B3, 17F6, 16F6, and 17F6.

[0022] A further embodiment relates to the complementary determining regions of these five antibodies (16H11, 19B3, 17F6, 16F6, and 17F6) which are involved with the binding of the monoclonal antibodies to Ebola Sudan Boniface virus.

[0023] Another embodiment of the invention relates to antibodies that are functionally equivalent to the antibodies listed above. These functionally equivalent antibodies substantially share at least one major functional property with an antibody listed above and herein described comprising: binding specificity to Ebola Sudan Boniface (ESB) GP, protection against ESB challenge when administered prophylactically or thera-